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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/921,380 | 08/02/2001 | Charles Mark Ensor | PHOE-0061 | 7237 |

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EXAMINER

PATTERSON, CHARLES L JR

ART UNIT PAPER NUMBER

1652

DATE MAILED: 04/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/921,380

Applicant(s)

ENSOR ET AL.

Examiner

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for PEG-5,000 or PEG-20,000 bound to uricase at unknown residues, does not reasonably provide enablement for claims of the scope of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

As stated previously, the specification teaches that when the methoxy-SS-polyethylene glycol derivation of PEG-5,000 or PEG-20,000 is used to PEG-ylate uricase from *Candida utilis*, the conjugate has a longer "circulating half-life" than the unmodified uricase while retaining about 56% to 75% of its activity. Applicants argue that the specification teaches on page 10, lines 13-18 and page 11, line 30 to page 12, line 3 that PEG of 15,000-30,000 molecular weight bound to uricase increases the circulating half-life. The instant teachings are general and the only specific teachings are in Table 1, where it is shown that uricase bound to PEG-5 and PEG-20 has increased circulating half-life and retains significant activity. There is no teaching as to exactly what effect binding uricase to PEG from 15,000 - 30,000 molecular weight will have. Applicants further argue that page 11, lines 22-23 states that "particular linking groups do not appear to influence the circulating half-life of PEG-uricase or its specific enzyme activity". Therefore the

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part of the previous scope rejection regarding which linking group was used is dropped in view of this teaching. Everything else addressed in applicant reply is addressed to now canceled claims and is moot.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gloger, et al. (BG) in view of either of Davis, et al. (A) or Zalipsky, et al. (AY). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants first argue that the statement in the previous action regarding increase in activity increase when enzyme is bound to PEG is not supported by the instant combination of references. This part of the rejection applied to claims 26-30 and since these claims have now been deleted, this argument is moot. Applicants do not argue anything regarding the teachings that coupling PEG to proteins substantially reduces the antigenicity of the conjugate. This is taught at least in column 2, lines 26-30 of Davis, et al. and at least in the second paragraph on page 347 of Zalipsky. The latter reference also teaches in the second paragraph on page 347 that attaching PEG increases the circulating half-life of the proteins. As stated previously,

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Gloger, et al. teach that uricase can be obtained from *Candida utilis* and *Aspergillus flavus*.

It would have been obvious to one of ordinary skill in the art to obtain the uricase from the source taught by Gloger, et al and to use PEGs of molecular weight 15,000 - 20,000 in view of the teaching of Davis, et al. and Zapilsky, et al. The motivation would have been to reduce antigenicity and/or to increase circulating half-life.

Claims 1-5, 8-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chua, et al. (AB) in view of either of Davis, et al. (A) or Zalipsky, et al. (AY). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

As stated previously, Chua, et al. teach that uricase can be obtained from *Arthrobacter protoformiae*. They also teach that attachment of PEG will lower the immunogenicity and prolong the circulating half life. The pertinent teachings of Davis, et al. and Zalipsky, et al. are discussed *supra* and in the previous action. It would have been obvious to one of ordinary skill in the art to obtain the uricase from the sources taught by Chua, et al. and to use PEGs of molecular weights 15,000 - 20,000 in view of the teachings of Davis, et al and Zalipsky, et al. The motivation would have been to reduce antigenicity and/or to increase circulating half-life.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a


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first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
April 25, 2003